09937875 .100102

533 Rec'd PCT/PTO 01 OCT 2001

FORM PTO-1390 REV. 5-93	US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEYS DOCKET NUMBER
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		P01,0337
		U.S.APPLICATION NO. (if known, see 37 CFR 1.5) 09/937875
INTERNATIONAL APPLICATION NO. PCT/SE00/00572	INTERNATIONAL FILING DATE 23 March 2000	PRIORITY DATE CLAIMED 31 March 1999

TLE OF INVENTION

A RATE ADAPTIVE PACEMAKER

APPLICANT(S) FOR DO/EO/US

MART MIN, ANDRES KINK and TOOMAS PARVE

pplicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay.
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of International Application as filed (35 U.S.C. 371(c)(2)) - drawings attached.
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2) -

7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.

8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98; **(PTO 1449, Prior Art, Search Report).**

12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included. (Separate envelope)

13. ☐ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.

14. ☐ A substitute specification, including red-lined version

15. ☐ A change of power of attorney and/or address letter.

16. ☒ Other items or information:
    a. ☐ Request for Approval of Drawing Changes

    B ☒ Express Mail Label EL 843741752US

410 Rec'd PCT/PTO 01 OCT 2001

U.S.APPLICATION NO. (if known, see 37 C.F.R. 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/937875	PCT/SE00/00572	P01,0337

17. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
BASIC NATIONAL FEE (37 C.F.R. 1.492(a)(1)-(5): Search Report has been prepared by the EPO or JPO $890.00		
International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) $710.00		
No international preliminary examination fee paid to USPTO (37 C.F.R. 1.482) but international search fee paid to USPTO (37 C.F.R. 1.445(a)(2) $740.00		
Neither international preliminary examination fee (37 C.F.R. 1.482) nor international search fee (37 C.F.R. 1.445(a)(2) paid to USPTO $1040.00		
International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) $100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$890.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. 1.492(e)).	$	

Claims	Number Filed		Number Extra	Rate		
Total Claims	13	- 20 =	0	X $18.00	$	
Independent Claims	1	- 3 =	0	X $ 84.00	$	
Multiple Dependent Claims				$280.00 +	$280.00	
				TOTAL OF ABOVE CALCULATIONS =	$1170.00	
Reduction by ½ for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 C.F.R. 1.9, 1.27, 1.28)					$	
				SUBTOTAL =	$1170.00	
Processing fee of $130.00 for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +					$	
				TOTAL NATIONAL FEE =	1170.00	
Fee for recording the enclosed assignment (37 C.F.R. 1.21(h). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28, 3.31). $40.00 per property +						
				TOTAL FEES ENCLOSED =	$1170.00	
				Amount to be refunded	$	
				charged	$	

a. ☒ A check in the amount of $1170.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 501519. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 C.F.R. 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Schiff Hardin & Waite
Patent Department
6600 Sears Tower
Chicago, Illinois 60606
Customer No. 26574

Steven H. Noll
SIGNATURE

Steven H. Noll
NAME

28,982 (Registration No.)

BOX PCT

IN THE UNITED STATES DESIGNATED OFFICE

OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

UNDER THE PATENT COOPERATION TREATY-CHAPTER II

AMENDMENT "A" PRIOR TO ACTION AND SUBMISSION OF SUBSTITUTE SPECIFICATION

APPLICANTS: Min et al.

SERIAL NO.: 09/937,875

FILED: October 1, 2001

TITLE: "A RATE ADAPTIVE PACEMAKER"

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

Applicants herewith amend the above-referenced PCT application as follows, and requests entry of the Amendment prior to examination in the United States National Examination Phase.

IN THE SPECIFICATION:

Please enter the substitute specification submitted herewith pursuant to 37 C.F.R. §1.125(b). The substitute specification is based on amended sheets 1, 2 and 3, filed during earlier PCT prosecution, and original sheets 4, 5 and 6. A marked-up copy showing all of changes made in the substitute specification is also submitted herewith. The substitute specification does not contain any new matter.

IN THE DRAWINGS:

Please amend each of Figures 1 and 2 as shown on the drawing copy marked in red attached to the Request for Approval of Drawing Changes, filed simultaneously herewith.

IN THE CLAIMS:

On amended sheet 7, in line 1, cancel "*Claims*" and substitute: --WE CLAIM AS OUR INVENTION-- therefor.

Cancel claims 1-6 on substitute sheets 7 and 8, and substitute the following claims therefor:

--7. A rate adaptive pacemaker comprising:

an arrangement adapted for interaction with a subject for obtaining an electrical signal representing cardiac demand of said subject;

a computing unit supplied with said signal for calculating an actual cardiac output CO, and a cardiac output CO_{rest} for said subject at rest;

a pacing rate controller also supplied with said signal for generating, as an output, a pacing rate dependent on said cardiac demand; and

a pacing rate limiter connected to said computing unit and to said pacing rate controller for downwardly limiting said pacing rate, said pacing rate limiter calculating a stroke volume SV and a stroke volume SV_{rest} for said subject at rest, and downwardly limiting said pacing rate so that a first predetermined relation $CO > CO_{rest}$ and a second predetermined relation $SV/SV_{rest} < L$ are satisfied, wherein L is a predetermined constant in a range between 1.2 and 1.5.

8. A rate adaptive pacemaker as claimed in claim 7 wherein said pacing rate limiter comprises a lower limit setting unit for setting a lower limit value for said pacing rate and a lower limit determining unit wherein SV and SV_{rest} are determined, and wherein a relation between CO and CO_{rest} and a relation between SV and SV_{rest} are determined, and for calculating a lower pacing rate limit value from said relations for supply to said limit setting unit.

9. A rate adaptive pacemaker as claimed in claim 8 wherein said lower limit determining unit includes a comparator for comparing SV/SV_{rest} to L to ensure that (SV/SV_{rest} < is satisfied, and for calculating said lower pacing rate limit value as a product of HR_{rest} and Sv_{rest}/SV), wherein HR_{rest} is a heart rate for said subject at rest, provided (SV/SV_{rest}) < L is satisfied.

10. A rate adaptive pacemaker as claimed in claim 7 wherein said arrangement for determining cardiac demand comprises a bioimpedance measuring unit adapted to measure a cardiac bioimpedance as a function of time as said signal representing cardiac demand.

11. A rate adaptive pacemaker as claimed in claim 7 wherein said arrangement for determining cardiac demand comprises an ECG measuring unit for generating an ECG signal as said signal representing cardiac demand.

12. A rate adaptive pacemaker as claimed in claim 7 wherein said arrangement for determining cardiac demand is a dynamic distance measuring unit which generates a distance signal as said signal representing cardiac demand.--

IN THE ABSTRACT:

Please add the Abstract as set forth on separately numbered page 7, attached hereto.

REMARKS:

The present Amendment makes changes editorial changes in the specification, drawings and claims, and adds an Abstract, to conform the present PCT application to the requirements of United States patent practice. No departure in the claim language of claims 7-12 presented herein, as

compared to original claims 1-6, has been made for the purpose of distinguishing any of claims 7-12 over the teachings of the prior art of record. Claims 7-12 are considered to have the same scope as original claims 1-6, and accordingly no difference in the claim language between those sets of claims is intended by the Applicants as a surrender of any of the subject matter encompassed within the scope of original claims 1-6.

Early consideration of the present PCT application is respectfully requested.

Submitted by,

Stan W. Noll (Reg. 28,982)

SCHIFF, HARDIN & WAITE
CUSTOMER NO. 26574
Patent Department
6600 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606
Telephone: 312/258-5790
Attorneys for Applicants.

BOX PCT

IN THE UNITED STATES DESIGNATED OFFICE

OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

UNDER THE PATENT COOPERATION TREATY-CHAPTER II

REQUEST FOR APPROVAL OF DRAWING CHANGES

APPLICANTS: Min et al.

SERIAL NO.: 09/937,875

FILED: October 1, 2001

TITLE: "A RATE ADAPTIVE PACEMAKER"

Assistant Commissioner for Patents,

Washington, D.C.

S I R:

Applicants herewith request approval of the drawing changes in each of Figures 1 and 2, as shown on the drawing copy marked in red attached hereto.

Submitted by,

Steven H. Noll (Reg. 28,982)

SCHIFF, HARDIN & WAITE
CUSTOMER NO. 26574
Patent Department
6600 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606
Telephone: 312/258-5790
Attorneys for Applicants.

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, United States Patent and Trademark Office, P.O. Box 2327, Arlington, Virginia 22202 on Jan. 18, 2002

Steven H. Noll

STEVEN H. NOLL

Fig. 1

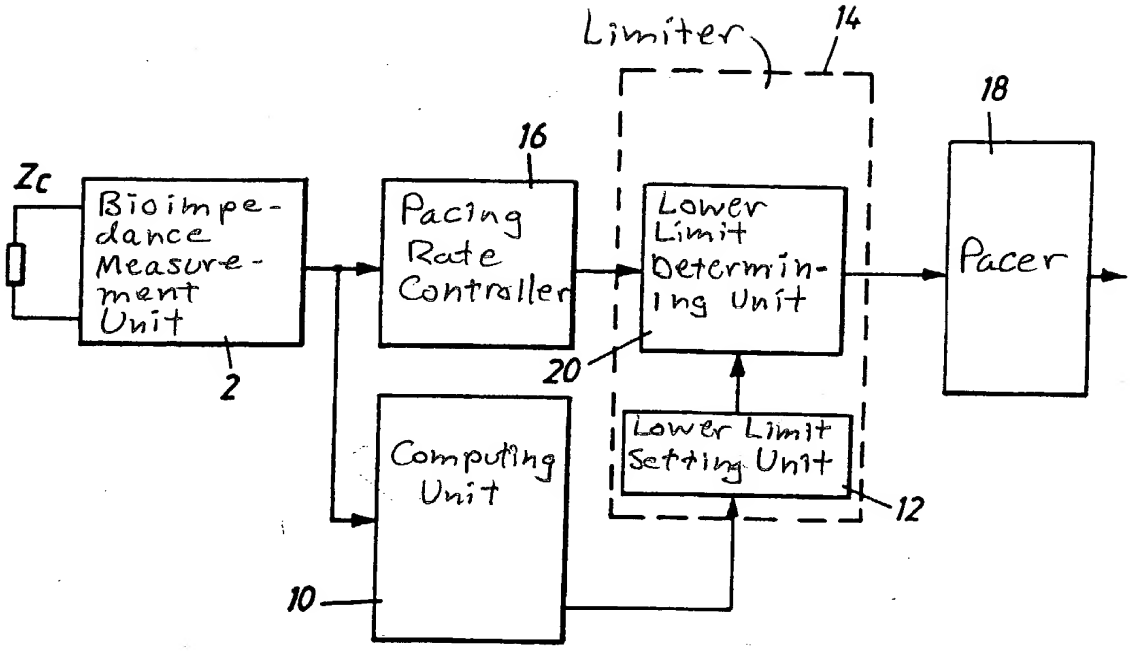
Limiter
14
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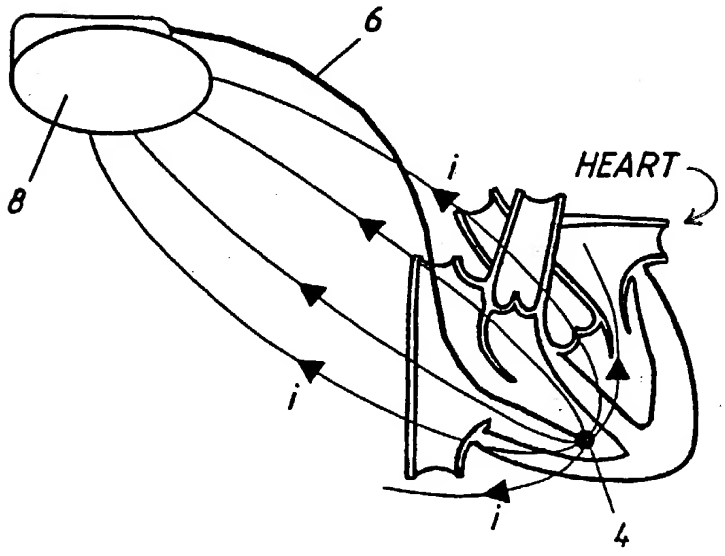
Fig. 2


6
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SUBSTITUTE SPECIFICATION

SPECIFICATION

TITLE

"A RATE ADAPTIVE PACEMAKER"

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a rate adaptive pacemaker of the type having an arrangement for determining the demand of the patient's organism, a pacing rate control for controlling the pacing rate in response to the patient's demand, and a pacing rate limiter for preventing the pacing rate from becoming too low.

Description of the Prior Art

The pacing rate of a rate adaptive pacemaker may become too low due to the physical demand of the patient's organism and heart. This may result in lack of oxygen supply to the myocardium. Under certain conditions the heart may not be able to fulfil the physiological needs of the patient's organism and heart if the pacing rate is not limited.

It is known to set a lower limit for the pacing rate. This limit value is normally determined from the patient's diagnosis and a constant or externally programmable limit can be set. Thus United States Patent No. 4,535,774 describes a stroke volume controlled pacemaker, in which the heart rate is permitted to range between prescribed minimum and maximum heart rate values. Further, in United States Patent No. 5,861,011 a pacemaker is disclosed having a system for determining the circadian rhythm by examining variations in the QT interval and adjusting the pacemaker night

time setting of a lower rate limit to the lower value than the pacemaker daytime setting of the lower rate limit. In United States Patent No. 5,183,040, an antitachycardia pacer is disclosed which analyzes cardiac output information for assessing hemodynamic status and determining adequate blood supply.

Thus, a pacing rate that is too low may cause an influx of blood enriched with oxygen that also is too low. A prescribed suitable lower pacing rate limit avoids the slow influx of the fresh blood. At the same time this lower limit value should be low enough so as to not to disturb a peaceful sleep. In that case the patient can feel more healthy in various everyday life conditions including peaceful sleeping.

SUMMARY OF THE INVENTION

An object of the present invention is to provide a rate adaptive pacemaker in which the pacing rate is prevented from becoming too low, such that the above discussed inconveniences for the patient are avoided.

The above object is achieved in accordance with the principles of the present invention in a rate adaptive pacemaker having an arrangement adapted for interaction with a subject for obtaining an electrical signal representing cardiac demand of the subject, a computing unit supplied with the signal for calculating an actual cardiac output CO and a cardiac output CO_{rest} for the subject at rest, a pacing rate controller also supplied with the signal for generating, as an output, a pacing rate dependent on the cardiac demand, and a pacing rate limiter connected to the computing unit and to the

pacing rate controller for downwardly limiting the pacing rate, wherein the pacing rate limiter calculates a stroke volume SV and a stroke volume SV_{rest} for the subject at rest, and downwardly limits the pacing rate so that a first predetermined relation $CO > CO_{rest}$ and a second predetermined relation $SV/SV_{rest} < L$ are satisfied, wherein L is a predetermined constant in a range between 1.2 and 1.5.

Thus, by satisfying two predetermined relations the pacemaker according to the invention ensures a sufficient minimum energy supply to the patient's organism or body and at the same time the maximum value of the stroke volume is limited and these conditions are continuously automatically checked.

In one embodiment of the pacemaker 20 according to the invention the first predetermined relation is

$$CO > {}_{Corest} \quad (1)$$

and the second predetermined relation is

$$(SV)/(SV_{rest}) < L \quad (2)$$

where L denotes a predetermined constant > 1, preferably equal to a value between 1.2 and 1.5. In this way it is ensured that the actual cardiac output will not become lower than the rest state cardiac output CO_{rest} as well as ensuring that the actual stroke volume will be less than a maximum allowed value equal to $L \times SV_{rest}$, where L typically has a value between 1.2 and 1.5, depending on the health of the patient's myocardium. By satisfying both

these conditions simultaneously a physiologically well founded heart work management at low work loads is ensured.

In another embodiment of the pacemaker according to the invention the pacing rate limiter includes a lower limit setting unit for setting a lower limit value for the pacing rate, and a lower limit determining unit for determining the relation between actual cardiac output (CO) and cardiac output (CO_{rest}) for the patent in rest conditions, and the relation between actual stroke volume (SV) and a rest stroke volume (SV_{rent}) and for calculating a lower pacing rate limit value from the relations for supply to said limit setting unit. The lower limit determining unit includes a stroke volume measuring unit for measuring actual stroke volume SV and a comparator for comparing measured actual stroke volume SV with stroke volume SV_{rest} for the patient in rest conditions to ensure that the inequality

$$SV/SV_{rest} < L \qquad (3)$$

is satisfied. The lower limit determining unit is adapted to calculate a lower pacing rate limit value from the equation

$$\text{lower pacing rate limit} = HR_{rest}\ (_{Svrest}/SV) \qquad (4)$$

where HR_{rest} denotes the heart rate for the patient in rest conditions, provided that said inequality is satisfied. In this way the lower pacing rate limit is continuously automatically calculated and it may also happen that the lower pacing rate limit becomes lower than the typical heart rate HR_{rest} for rest conditions of the patient.

In another embodiment of the pacemaker according to the invention a bioimpedance measurement unit is provided to measure the cardiac bioimpedance as a function of time for determining therefrom actual cardiac output CO and actual stroke volume SV from the measured cardiac bioimpedance. These parameters thus are obtained in an easy and reliable way from the time variation of the bioimpedance measured between a standard intracardiac electrode and the housing of the pacemaker, when an excitation current proceeds from the electrode tip.

DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic block diagram of a rate adaptive pacemaker constructed and operating in accordance with the principles of the present invention.

Figure 2 illustrates the principle of bioimpedance measurements between the tip of an intracardial electrode and the metallic housing of the pacemaker, these measurements being used in the rate adaptive pacemaker of Figure 1.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

To avoid the current cardiac output CO

$$CO = SV \times HR \tag{5}$$

becomes lower than the rest state cardiac output CO_{rest} the pacing rate must be above a lower pacing rate limit given by

$$\text{lower pacing rate limit} = (_{Corest})/(SV) \tag{6}$$

and since

$$CO_{rest} = HR_{rest} \times SV_{rest} \quad (7)$$

$$\text{lower pacing rate limit} = (HR_{rest}) \times (SV_{rest}/SV) \quad (8)$$

In addition the maximum value of the stroke volume must be limited, i.e.

$$SV < L \times SV_{rest} \quad (9)$$

Thus, the following two conditions must be fulfilled simultaneously for insuring a physiologically well founded heart work management at low work loads.

$$\text{Pacing rate limit} > (HR_{rest}) \times (SV_{rest}/SV) \quad (10)$$

$$SV/SV_{rest} < L \quad (11)$$

where L is a constant typically equal to a value of 1.2 to 1.5, depending on the health of the patient's myocardium.

Thus the lower pacing rate limit is continuously automatically calculated from the measured actual stroke volume SV and known values of SV_{rest}, HR_{rest} and the constant L. The actual stroke volume can be determined from e.g. bioimpedance measurements as will be described below.

Figure 1 is a block diagram of an embodiment of the pacemaker according to the invention having a bioimpedance measurement unit 2 for measuring the time variation of the electric intracardiac bioimpedance $Z_e(t)$. This type of measurement is well- known, see e.g. "Design of Cardiac Pacemakers", edited by John G. Webster, IEEE Press, 1995, pp. 380-386 and United States Patent Nos. 5,154,171, 5,280,429, 5,282,840 and

5,807,272. Thus the time variation of the intracardiac bioimpedance can be measured between the tip 4 of the intracardiac electrode 6 and the housing 8 of the pacemaker, when an excitation current is fed from the electrode tip 4, as schematically illustrated in Figure 2. Thus a standard pacing lead can be used for this measurement.

From the measured time variations AZc(t) the stroke volume SV needed for calculating the lower pacing rate limit according to equation (8) above, or for checking the inequalities (10) or (11), are determined in a computing unit 10, see Figure 1.

The calculated lower limit value is supplied to a lower limit 30 setting unit 12 of a pacing rate limiter 14.

A pacing rate controller 16 is also provided for controlling the pacing rate of the pacer or pulse generator 18 in response to the patient's demands. In a limiting unit 20 of the limiter 14 the demanded pacing rate is compared to the set lower limit pacing rate and the actual pacing rate is limited to the set lower limit value if the demanded pacing rate reaches this limit value. Thus in the pacemaker according to the invention a lower limit value for the pacing rate is continuously automatically determined and it is continuously automatically verified that the actual pacing rate does not exceed the present lower limit value.

Alternatively, the pacemaker can be modified to continuously monitor that the inequalities (10) or (11) above are satisfied.

Above bioimpedance measurements are described for determining the stroke volume SV. This parameter can, however, also be determined by other techniques, like by ECG measurements, by ultrasound technique, by radiometric and optical techniques etc. Generally all dynamic distance and/or capacity measuring methods are applicable.

Although modifications and changes may be suggested by those skilled in the art, it is the intention of the inventors to embody within the patent warranted hereon all changes and modifications as reasonably and properly come within the scope of their contribution to the art.

Technical Field

The present invention relates to a rate adaptive pacemaker comprising a means for determining the demand of the patient's organism, a pacing rate controlling means for controlling the pacing rate in response to the patient's demand, and a pacing rate limiting means for preventing the pacing rate from becoming too low.

Background Art

The pacing rate of a rate adaptive pacemaker may become too low due to the physical demand of the patient's organism and heart. This may result in lack of oxygen supply to the myocardium. Under certain conditions the heart may not be able to fulfil the physiological needs of the patient's organism and heart if the pacing rate is not limited.

It is previously known to set a lower limit for the pacing rate. This limit value is normally determined from the patient's diagnosis and a constant or externally programmable limit can be set. Thus US-A-4,535,774 describes a stroke volume controlled pacemaker, in which the heart rate is permitted to range between prescribed minimum and maximum heart rate values. Further, in US-A-5,861,011 a pacemaker is disclosed having a system for determining the circadian rhythm by examining variations in the QT interval and adjusting the pacemaker night time setting of a lower rate limit to a lower value than the pacemaker daytime setting of the lower rate limit. In US-A-5,183,040, an antitachycardia pacer is disclosed which analyzes cardiac output information for assessing hemodynamic status and determining adequate blood supply.

Thus, too low a pacing rate may cause too slow influx of blood enriched with oxygen. A prescribed suitable lower pacing rate limit avoids the slow influx of the fresh blood. At the same time this lower limit value should be low enough

not to disturb a peaceful sleep. In that case the patient can feel more healthy in various everyday life conditions including peaceful sleeping.

The purpose of the present invention is to provide a rate adaptive pacemaker in which the pacing rate is prevented in a new way from becoming too low, such that the above discussed inconveniences for the patient are avoided.

Disclosure of the Invention

This purpose is obtained by a rate adaptive pacemaker according to claim 1.

Thus, by satisfying two predetermined relations the pacemaker according to the invention ensures a sufficient minimum energy supply to the patient's organism or body and at the same time the maximum value of the stroke volume is limited and these conditions are continuously automatically checked, and where the first predetermined relation is

$$CO > CO_{rest} \quad (1)$$

and said second predetermined relation is

$$(SV)/(SV_{rest}) < L \quad (2)$$

where L denotes a predetermined constant equal to a value between 1.2 and 1.5. In this way the actual cardiac output is ensured not to become lower than the rest state cardiac output CO_{rest} and the actual stroke volume is ensured to be less than a maximum allowed value equal to $L \times SV_{rest}$, where L typically has a value between 1.2 and 1.5, depending on the health of the patient's myocardium. By satisfying both these conditions simultaneously a physiologically well founded heart work management at low work loads is ensured.

Preferred embodiments are set forth in the dependent claims.

According to advantageous embodiments of the pacemaker according to the invention the pacing rate limiting means includes a lower limit setting means for setting a lower limit value for the pacing rate, and a lower limit determining means for determining the relation between actual cardiac output (CO) and cardiac output (CO_{rest}) for the patent in rest conditions, and the relation between actual stroke volume (SV) and a rest stroke volume (SV_{rest}) and calculating a lower pacing rate limit value from said relations for supply to said limit setting means, and said lower limit determining means includes a stroke volume measuring means for measuring actual stroke volume SV and comparison means for comparing measured actual stroke volume SV with stroke volume SV_{rest} for the patient in rest conditions to ensure that the inequality

$$SV/SV_{rest} < L \qquad (3)$$

is satisfied and said lower limit determining means is adapted to calculate a lower pacing rate limit value from the equation

$$\text{lower pacing rate limit} = HR_{rest} \cdot (SV_{rest}/SV) \qquad (4)$$

where HR_{rest} denotes the heart rate for the patient in rest conditions, provided that said inequality is satisfied. In this way the lower pacing rate limit is continuously automatically calculated and it may also happen that the lower pacing rate limit becomes lower than the typical heart rate HR_{rest} for rest conditions of the patient.

According to another advantageous embodiment of the pacemaker according to the invention a bioimpedance measurement unit is provided to measure the cardiac bioimpedance as a function of time for determining therefrom actual cardiac output CO and actual stroke volume SV from the measured cardiac bioimpedance. In this way these parameters are obtained in an easy and reliable way from the time variation of the bioimpedance measured between a standard intracardiac

electrode and the housing of the pacemaker, when an excitation current proceeds from the electrode tip.

Brief Description of the Drawings

The invention will now be described more in detail with reference to the enclosed drawings on which figure 1 is a block diagram of an embodiment chosen as an example of the pacemaker according to the invention and figure 2 illustrates the principle of bioimpedance measurements between the tip of an intracardial electrode and the metal housing of the pacemaker.

Description of a Preferred Embodiment

To avoid that the current cardiac output CO

$$CO = SV \times HR \quad (5)$$

becomes lower than the rest state cardiac output CO_{rest} the pacing rate must be above a lower pacing rate limit given by

$$\text{lower pacing rate limit} = (CO_{rest})/(SV) \quad (6)$$

and since

$$CO_{rest} = HR_{rest} \times SV_{rest} \quad (7)$$

$$\text{lower pacing rate limit} = (HR_{rest}) \times (SV_{rest}/SV) \quad (8)$$

In addition thereto the maximum value of the stroke volume must be limited, i.e.

$$SV < L \times SV_{rest} \quad (9)$$

Thus, the following two conditions must be fulfilled simultaneously for insuring a physiologically well founded heart work management at low work loads.

$$\text{Pacing rate limit} > (HR_{rest}) \times (SV_{rest}/SV) \quad (10)$$

$$SV/SV_{rest} < L \quad (11)$$

where L is a constant typically equal to a value of 1.2 to 1.5, depending on the health of the patient's myocardium.

Thus the lower pacing rate limit is continuously automatically calculated from the measured actual stroke volume SV and known values of SV_{rest}, HR_{rest} and the constant L. The actual stroke volume can be determined from e.g. bioimpedance measurements as will be described below.

Figure 1 is a block diagram of an embodiment of the pacemaker according to the invention comprising a bioimpedance measurement unit 2 for measuring the time variation of the electric intracardiac bioimpedance $Z_c(t)$. This type of measurements is well known, see e.g. "Design of Cardiac Pacemakers", edited by John G. Webster, IEEE Press, 1995, pp. 380-386 and US-A-5,154,171, 5,280,429, 5,282,840 and 5,807,272. Thus the time variation of the intracardiac bioimpedance can be measured between the tip 4 of the intracardiac electrode 6 and the housing 8 of the pacemaker, when an excitation current is fed from the electrode tip 4, as schematically illustrated in figure 2. Thus a standard pacing lead can be used for this measurement.

From the measured time variations $\Delta Z_c(t)$ the stroke volume SV needed for calculating the lower pacing rate limit according to equation (8) above, or for checking the inequalities (10) or (11), are determined in computing means 10, see figure 1.

The calculated lower limit value is supplied to a lower limit setting means 12 of a pacing rate limiter 14.

A pacing rate controller 16 is also provided for controlling the pacing rate of the pacer or pulse generator 18 in response to the patient's demands. In a limiting unit 20 of the limiter 14 the demanded pacing rate is compared to the set lower limit pacing rate and the actual pacing rate is limited to the set lower limit value if the demanded pacing

rate reaches this limit value. Thus in the pacemaker according to the invention a lower limit value for the pacing rate is continuously automatically determined and it is continuously automatically verified that the actual pacing rate does not exceed the present lower limit value.

Alternatively, the pacemaker can be modified to continuously monitor that the inequalities (10) or (11) above are satisfied.

Above bioimpedance measurements are described for determining the stroke volume SV. This parameter can, however, also be determined by other techniques, like by ECG measurements, by ultrasound technique, by radiometric and optical techniques etc. Generally all dynamic distance and/or capacity measuring methods are applicable.

Claims

1. A rate adaptive pacemaker comprising a means (2) for determining the demand of the patient's organism, a pacing rate controlling means (16) for controlling the pacing rate in response to the patient's demand, and a pacing rate limiting means (14) for preventing the pacing rate from becoming too low, said pacing rate limiting means (14) being adapted to limit the pacing rate downwards such that a first predetermined relation is satisfied between actual cardiac output (CO) and cardiac output (CO_{rest}) for the patient in rest conditions and a second predetermined relation is satisfied between actual stroke volume (SV) and rest stroke volume (SV_{rest}), **characterized in** that said first predetermined relation is

$$CO > CO_{rest}$$

and said second predetermined relation is

$$(SV)/(SV_{rest}) < L$$

where L denotes a predetermined constant equal to a value between 1.2 and 1.5.

2. The pacemaker according to claim 1, **characterized in** that said pacing rate limiting means (14) includes a lower limit setting means for setting a lower limit value for the pacing rate, and a lower limit determining means (10) for determining the relation between actual cardiac output (CO) and cardiac output (CO_{rest}) for the patient in rest conditions and the relation between actual stroke volume (SV) and a rest stroke volume (SV_{rest}) and calculating a lower pacing rate limit value from said relations for supply to said limit setting means.

3. The pacemaker according to claim 2, **characterized in** that said lower limit determining means (10) includes a stroke volume measuring means for measuring actual stroke volume SV and comparison means for comparing measured actual

stroke volume SV with stroke volume SV_{rest} for the patient in rest conditions to ensure that the inequality

$$SV/SV_{rest} < L$$

is satisfied, and in that said lower limit determining means (10) is adapted to calculate a lower pacing rate limit value from the equation

$$\text{lower pacing rate limit} = HR_{rest} \cdot (SV_{rest}/SV)$$

where HR_{rest} denotes the heart rate for the patient in rest conditions, provided that said inequality is satisfied.

4. The pacemaker according to any of the claims 1-3, **characterized in** that a bioimpedance measurement unit (2) is provided to measure the cardiac bioimpedance as a function of time for determining therefrom actual cardiac output (CO) and actual stroke volume (SV) from the measured cardiac bioimpedance.

5. The pacemaker according to any of the claims 1-3, **characterized in** that an ECG measuring and analyzing unit is provided to measure ECG and determine therefrom actual cardiac output (CO) and actual stroke volume (SV).

6. The pacemaker according to any one of claims 1-4, **characterized in that** a dynamic distance measuring and analyzing unit is provided to determine therefrom actual cardiac output (CO) and actual stroke volume (SV).

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(71) Applicant *(for all designated States except US)*: PACESETTER AB [SE/SE]; S-175 84 Järfälla (SE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: MIN, Mart [EE/EE]; Söpruse pst. 188A-4, EE-Tallinn (EE). KINK, Andres [EE/EE]; Nabala tee 2A, Kiili, EE-75401 Harjumaa (EE). PARVE, Toomas [EE/EE]; Rännaku blvd. 3-7, EE-10917 Tallinn (EE).

(74) Common Representative: PACESETTER AB; Patent Department, Att: Sven Kalling, S-175 84 Järfälla (SE).

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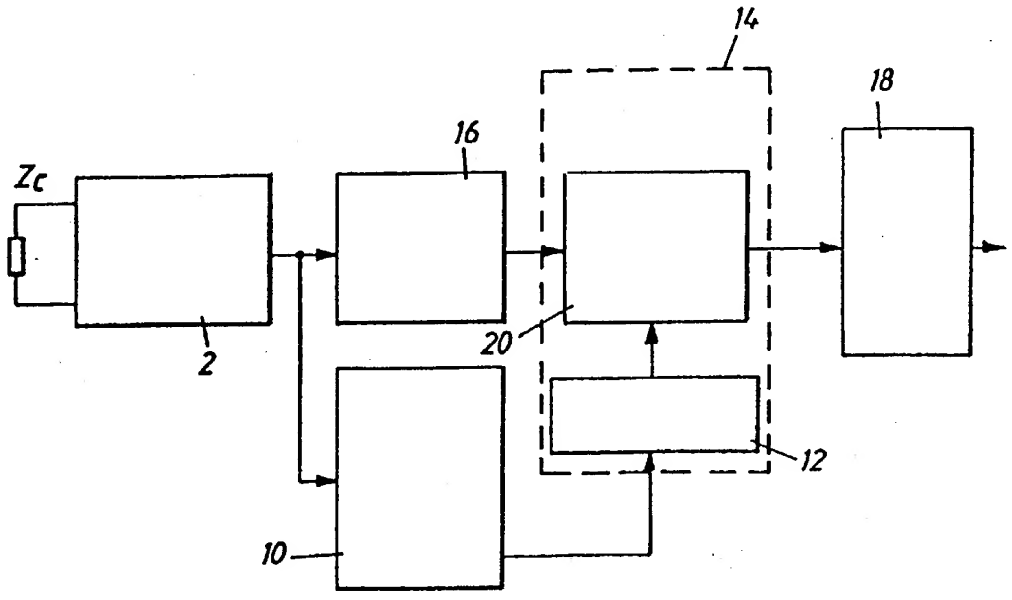


(57) Abstract

A rate adaptive pacemaker comprises a means (2) for determining the demand of the patient's organism, a pacing rate controlling means (16) for controlling the pacing rate in response to the patient's demand, and a pacing rate limiting means (20) for preventing the pacing rate from becoming too low. The pacing rate limiting means is adapted to limit the pacing rate downwards such that a first predetermined relation is satisfied between actual cardiac output (CO) and cardiac output (CO_{rest}) for the patient in rest conditions and a second predetermined relation is satisfied between actual stroke volume (SV) and rest stroke volume (SV_{rest}).

Fig. 1

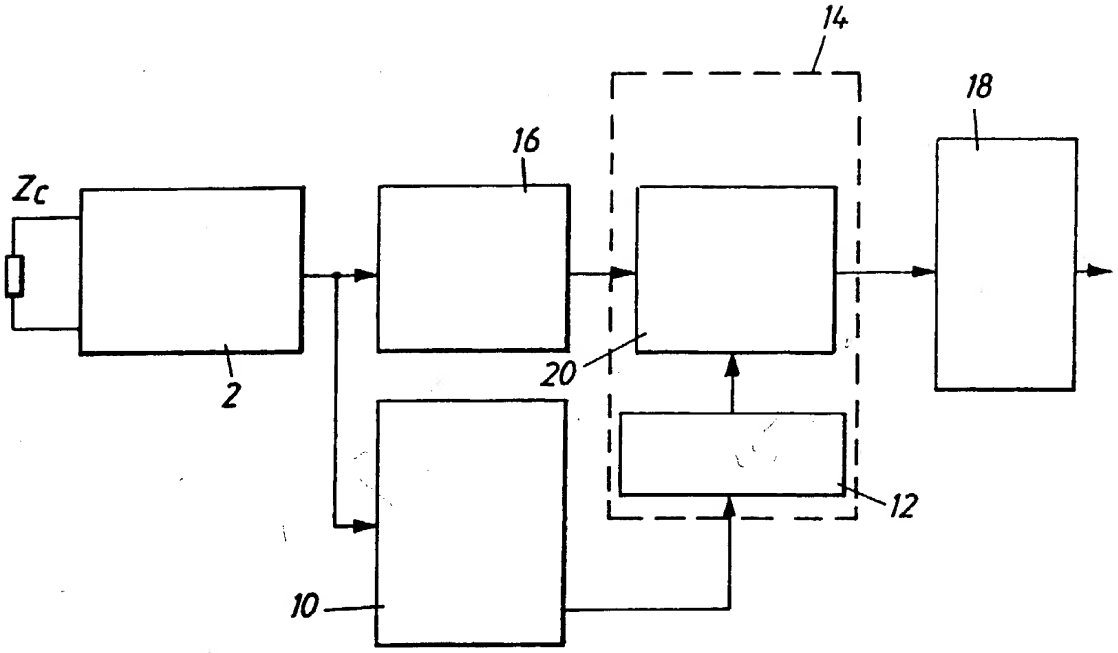
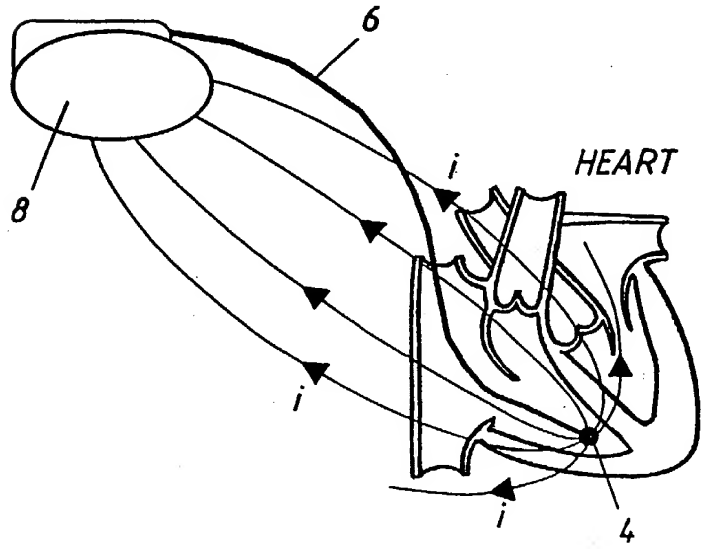


Fig. 2



COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Includes Reference to PCT International Applications)	ATTORNEY'S DOCKET NUMBER P01,0337

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

"A RATE ADAPTIVE PACEMAKER"

the specification of which (check only one item below):

☐ is attached hereto.

☐ was filed as United States application
Serial No. ______________________

on ______________________

and was amended

on ______________________(if applicable).

■ was filed as PCT international application

Number ______ PCT/SE00/00572

on ______ March 23, 2000

and was amended under PCT Article 19

on ______________________(if applicable).

I hereby state that I have reviewed and understand the content of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

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COUNTRY (if PCT (indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
Sweden	9901194-2	31.03.99	■ YES ☐ NO
			☐ YES ☐ NO
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			☐ YES ☐ NO
			☐ YES ☐ NO

Combined Declaration For Patent Application and Power of Attorney (Continued)
(Includes Reference to PCT International Applications)

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Send Correspondence to: SCHIFF, HARDIN & WAITE
Patent Department
6600 Sears Tower, Chicago, Illinois 60606
Customer Number 26574

Direct Telephone Calls to:
312/258-5790

201	FULL NAME OF INVENTOR	FAMILY NAME: MIN	FIRST GIVEN NAME: MART	SECOND GIVEN NAME
	RESIDENCE & CITIZENSHIP	CITY: Tallinn	STATE OR FOREIGN COUNTRY: Estonia EEX	COUNTRY OF CITIZENSHIP: Estonia
	POST OFFICE ADDRESS	POST OFFICE ADDRESS: Sopruse pst 155A-4	CITY: Tallinn	STATE & ZIP CODE/COUNTRY: EE13424 Tallinn, Estonia
202	FULL NAME OF INVENTOR	FAMILY NAME: KINK	FIRST GIVEN NAME: ANDRES	SECOND GIVEN NAME
	RESIDENCE & CITIZENSHIP	CITY: Harjumaa	STATE OR FOREIGN COUNTRY: Estonia EEX	COUNTRY OF CITIZENSHIP: Estonia
	POST OFFICE ADDRESS	POST OFFICE ADDRESS: Nabala tee 2A	CITY: Harjumaa	STATE & ZIP CODE/COUNTRY: EE76401 Harjumaa, Estonia
203	FULL NAME OF INVENTOR	FAMILY NAME: PARVE	FIRST GIVEN NAME: TOOMAS	SECOND GIVEN NAME
	RESIDENCE & CITIZENSHIP	CITY: Tallinn	STATE OR FOREIGN COUNTRY: Estonia EEX	COUNTRY OF CITIZENSHIP: Estonia
	POST OFFICE ADDRESS	POST OFFICE ADDRESS: Rahnaku blvd 3-7	CITY: Tallinn	STATE & ZIP CODE/COUNTRY: EE10917 Tallinn

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SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
M. Min	A. Kink	T. Parve
DATE Sept. 26, 2001	DATE Sept 26, 2001	DATE Sept. 26, 2001

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